IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Peled et al.	CONF NO.:	9770
SERIAL NUMBER:	10/774,843	EXAMINER :	Maria Gomez Leavitt
FILING DATE:	February 9, 2004	ART UNIT :	1633
FOR:	EXPANSION OF RENEWABLE STEM CELL POPULATIONS		

Via EFS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DR. TONY PELED UNDER 37 C.F.R. §1.132

I, Tony Peled, declare and state that:

1. I received a Ph.D. degree from the Hebrew University - Hadassah Medical School in Jerusalem, Israel. I am the Chief Scientist, Vice President and co-founder of Gamida Cell Ltd. of Jerusalem, Israel (the Assignee of the above-referenced application). A principal aspect of my research is the study of stem cell culture and the therapeutic application of stem cell technology. I am the author of numerous peer-reviewed publications and posters, most of which are directed to cell expansion and cell differentiation, with specific focus on hematopoietic stem cells.

2. I have reviewed the Office Action dated September 21, 2009. I understand that claims 401, 411, 414, 416, 419, 422-424, 437, 438, 464, 465, 469-471 and 478-480 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US Patent Publication No. 2002/0159984 to Brown ("Brown") over U.S. Patent No. 6,413,772 to Block ("Block"). I also understand that claims 437 and 438 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brown and Block and further in view of Banasik *et al.*, 1992 JBC, 1569-1575 ("Banasik").

3. I have reviewed the accompanying amendment and the above-referenced application in conjunction with the cited references.

4. I have described below experiments that demonstrate that culturing CD34+ hematopoietic stem cells *ex-vivo* under conditions allowing for cell proliferation where a growth medium which contains nutrients, serum and a combination of cytokines including stem cell factor, thrombopoietin, FLt3 ligand, IL-6 and optionally IL-3 and in the same culture medium providing nicotinamide in an amount between 1.0 mM to 10 mM, results in a cell population that is expanded in the population of CD34+ hematopoietic stem cells with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as compared to CD34+ cells cultured in the presence of cytokines and nutrients without exogenously added nicotinamide. The CD34+ hematopoietic stem cells of the present invention can also be cultured under these conditions and further include IL-3.

5. Figure 1 attached hereto shows the results obtained by culturing CD34+ hematopoietic stem cells *ex-vivo* in culture with serum and a combination of the 4 claimed cytokines (FLT3, IL-6, TPO and SCF, 50ng/m, each), either without nicotinamide or with an increasing concentration of nicotinamide (within the claimed range of 1.0 mM to 10.0 mM). Cultured cells were counted on day 7, 14 and 21 day post seeding and FACS analyzed to determine percentages of CD34+ cells. This data demonstrates that culturing in a growth media including stem cell factor, thrombopoietin, FLt3 ligand and IL-6 in the presence of serum and nicotinamide results in a cell population that is expanded in the population of CD34+ hematopoietic stem cells with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as compared to CD34+ cells cultured in the presence of cytokines and nutrients without exogenously added nicotinamide.

6. Figure 2 attached hereto shows the results obtained by culturing CD34+ hematopoietic stem cells *ex-vivo* in culture with serum and a combination of the 4 claimed cytokines (FLT3, IL-6, TPO and SCF, 50ng/m, each) and additionally IL-3, either without nicotinamide or with an increasing concentration of nicotinamide (within the claimed range of 1.0 mM to 10.0 mM). Cultured cells were analyzed 7, 14 and 21 post seeding for total number of cells. This data demonstrates that culturing in a growth media including stem cell factor, thrombopoietin, FLt3 ligand, IL-6 and additionally IL-3 in the presence of serum and nicotinamide results in a cell population that is expanded in the population of CD34+ hematopoietic stem cells with an increased proportion of CD34+/Lin- and CD34+/CD38- cells in the expanded culture as

compared to CD34+ cells cultured in the presence of cytokines and nutrients without exogenously added nicotinamide.

7. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Tony Peled, Ph.D.

Signed this 22 day of February, 2010

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gamida cell

Dose response effect of NAM on CD34+ cell cultures

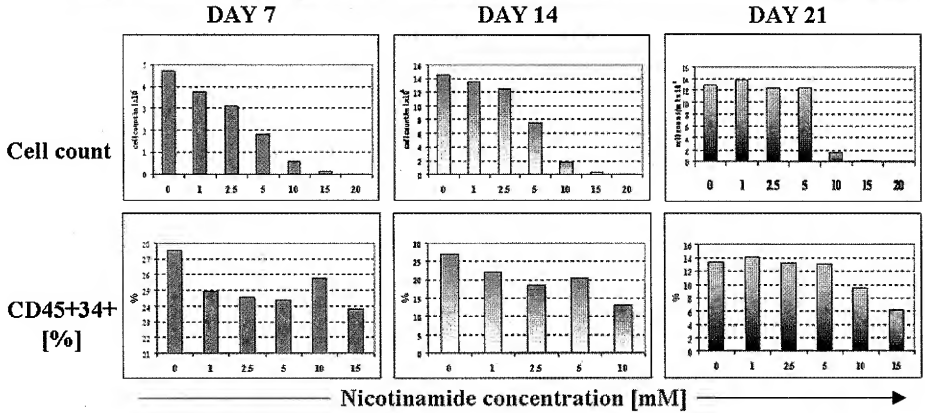

Figure 1

gamida cell

The effect of NAM on CD34+ cell cultured with IL-3

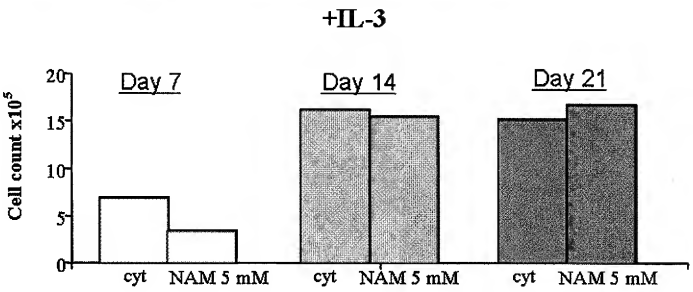

Figure 2